HUMAN TEMPERATURE REGULATION UNDER SPINAL ANESTHESIA

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DEDICATION

For...

Parents who encouraged

Francis who tutored

and

Susan who lived through it all

Introduction

The ability of the homeotherm to control internal body temperature despite wide variations in ambient temperature and levels of physical activity has been an active field of research since before the turn of the century. Ability to control internal temperature is one of the evolutionary milestones that enabled ancestoral "man" to emerge from the seas and populate much of the earth's land mass. He who has seen the alligator move into a pond, or the snake crawl under a rock to escape the killing noontime sun realizes the adaptability inherent in auto-temperature regulation. Yet our knowledge of actual temperature regulation mechanisms was largely sketchy until the work of physicists and systems analysts during the past two decades. Using the tools of neurophysiology and computor science, these modern temperature regulation researchers have put the flesh of systems models on the skeleton of descriptive physiology.

My interest in the field of temperature regulation studies was kindled when I saw post-operative patients shivering violently despite seemingly adequate bedclothing. That these patients were in pain I could understand; that they were "cold" I could not. Fortunately at that time, I had as my surgical mentor Dr. C. Francis Roe, who, I learned later, has published a number of research papers on the effects of anesthesia on temperature regulation. He referred me to the appropriate literature and continued to work with me as I approached some understanding of the topic. Such was the very beginnings of this thesis.

The modern literature on temperature regulation is highlighted by the studies which have come out of the John B. Pierce Foundation. References to these studies by scientists such as L. P. Herrington, J. D. Hardy, H. T. Hammel, and J. A. J. Stolwijk are throughout this thesis, and make

stimulating and exciting reading. Dr. Hardy offered me his advice and salutations for which I am grateful.

A word about the organization of this thesis. An historical review of temperature regulation studies is briefly presented followed by a more detailed examination of the work of the past decade on the elucidation of control mechanisms governing homeotherm responses to changes in internal and ambient temperatures. Spinal anesthesia is then discussed so as to better understand the rationale for its selection as an acute experimental model in temperature regulation studies. Experimental protocol, resultant data, and discussion follow.

I wish to express my thanks to Dr. C. Francis Roe for his advice, assistance, criticism, and his unflagging good nature. It has been my good fortune and pleasure to work with him on this project.

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Literature Review

That the central nervous system plays a role in homeotherm temperature regulation was first demonstrated by Richet in Paris and Ott[34] in Philadelphia. Ott, in 1884, experimented with rabbits making "punctures of the brain" and observed changes in the ability of the animal to regulate its internal temperature. Brain punctures at "the anterior inner-end of the optic thalami...causes an increase of temperature due to increased heat production". The significance of this finding was appreciated though not understood: "We have here", said Ott, "an artificial fever due to nervous disturbance, and not to any poisons circulating in the blood...a rise of 7 degrees Fahrenheit in an hour.... As to the nature of these centres, all opinions are more or less conjectural."

Building upon the pioneering work of researchers such as Ott, Sir Charles Sherrington made a number of pertinent observations concerning temperature regulation. His model was the spinal dog after subsidence of post-transection spinal shock. No "brain punctures" were utilized.

Post spinal shock spinal dogs show disturbances in temperature regulatory mechanisms. Before examining the specific disturbances, the experimental model must be clarified in terms of input and output. The obvious historical anachronism is noted but, nevertheless, presented.

1. Spinal cord transection interrupts afferent signals concerning temperature sensation (see later for work concerning afferent input from cold and warm receptors) below the level of transection.
2. Spinal cord transection interrupts thermoregulatory heat conserving and dissipating neural pathways. Effector output is thus inhibited.

3. Sympathetic outflow is at least partially interrupted in the acute spinal dog preparation. "The skin... is well warm, even to the tips of the hands and feet"[47] during the period of spinal shock, but a variable degree of vasomotor tone returns post spinal shock. Thus sympathetic tone may be intact or partially dampened in the chronic preparation. (See later work concerning the effects of sympathectomy alone on temperature regulation.)
4. The brain is intact, or, as Sherrington writes so beautifully, "the sudden cutting off of that stream of subconscious centripetal impulses which must be continually pouring to the brain from tail, lower limbs and trunk seems to disturb the head and brain not at all".[47]

Given this guideline to the chronic spinal dog preparation, the experimental data may be presented and interpreted.

"In dogs long after complete subsidence of spinal shock as judged from usual post-transection reflexes, there persists in the region innervated from behind the transection marked failure of adjustment of the surface blood supply (paws, pinnae, nose) to changes of surrounding cold and warmth. The failure of this vascular adjustment, though not absolute, remains severe and without improvement. Along with it there is complete abeyance of sweating to heat, and in the muscles complete abeyance of shivering to cold. Diurnal fluctuation of 2°C in the stall temperature affected conspicuously the vaginal temperature of cervical paraplegic dogs fully recovered from spinal shock."[46]

The failure of vascular adjustments, sweating, and shivering to temperature changes clearly, at the very least, represents defects in motor effector mechanisms for temperature regulation. That sensory blockade to peripheral temperature sensation plays a role is a more difficult inference to substantiate. Sherrington also chilled the insentient portion of the spinal dog while keeping the sentient segment warm and noted that the sentient portion shivered. He hypothesized a "deep origin" for the shiver response "from direct cooling of a central (diencephalic) thermotaxic mechanism."[46]

Sherrington's work on temperature regulation, though limited, is important. The "heat centre in the brain" of Ott began to assume some functional significance in thermoregulation. Although afferent signals to such a "deep center" were not elucidated, motor effector elements for heat conservation (i.e., shivering) and heat dissipation (i.e., sweating) became appreciated as possible outputs from a temperature regulation center.

The hypothalamus was firmly localized as the thermoregulatory center in the brain largely through numerous ablation studies in the 1930's. Electrical or thermal ablations in defined sectors of the hypothalamus resulted in impaired thermal adaptation to heat and cold stresses. Large hypothalamic lesions destroyed the animals' capacity to maintain body temperature even without ambient stress.

The role of the sympathetic nervous system in coping with changes in ambient temperatures was explored by Sawyer et. al..[44] Sympathetic outflow is a well known reaction to stress. An intact sympathetic signal would trigger such variable end-organ responses, depending upon the type and intensity of stress as:

1. Adrenal medullary secretions of calorigenic epinephrine

2. Vasoconstriction, most conspicuously in the skin and subcutaneous tissues and splanchnic bed
3. Sweat gland secretions via cholinergic sympathetic discharge

Sawyer sympathectomized cats and compared these cats to normal feline controls under heat and cold stress. The sympathectomized cats showed wider variation in core temperatures than did the controls, both under cold and heat stress.

Warm Exposure (40°C for 2 hours)

	Control Cats	Sympathectomized Cats
average temperature pre:	38.5° - 39°C	38.5° - 39°C
average temperature post:	40° - 40.5°C	41°C
average increase:	+1.40°C	+2.25°C

Cold Exposure (9° C for 24 hours)

	Control Cats	Sympathectomized Cats
average change:	up 0.4°C	down 1.63°C

Sympathectomy obviously interfered with heat dissipating mechanisms in cats under heat stress. Loss of sympathetic outflow also inhibited the calorigenic response to cold exhibited by the normal cats. An intact sympathetic nervous system is thus seen as one physiologic mechanism contributing to the preservation of thermal homeostasis under stressful extremes in ambient temperature.

In a review of temperature regulation research published prior to 1942, Herrington and Gagge[28] summarized what was known in the field to that date. Descriptive work in cold stress was singularly panned: "at the pres-

ent time it cannot be said that either the animal experiments in hypothermia or the more hazardous adventures in cold therapy with humans have greatly extended our knowledge of heat regulation". On the sensory input into the hypothalamic temperature regulatory system, a qualitative statement is offered: "heated blood acting on the central nervous system is the cause of generalized sweating. Whether the heated blood acts directly on the heat centers or by liberating some hormone which, in turn, stimulates the centers is uncertain".

In contrast to the early qualitative analyses of temperature regulation research, the work of the past two decades in the field of thermoregulation has been quantitative, rigorous and insightful. Experimentation has focused on defining temperature sensing input into the hypothalamic integrative thermoregulatory mechanism, hypothalamic-triggered effector response, and the mechanism of action of the hypothalamic "thermostat" itself. Much of this basic research has come out of the John B. Pierce Foundation Laboratories. The engineering concept of systems analysis as applied to a biophysical problem has proven fruitful in gaining our present understanding of homeotherm temperature regulation.

The problem of defining the relationship between peripheral and central responses to environmental temperature was investigated by Davis.[4] This study on mice concerned itself with shivering as quantified by electromyographically amplified muscle action potentials. The central nervous system was intact; ambient temperatures were varied. The results of the study indicated that within a core temperature range closely approximating normal, the biggest variable as to whether the mice would shiver was the skin temperature. Once core temperatures varied further from this normal range, the primary drive to shiver was centrally mediated and did not depend upon

skin temperature.

This study points toward a model of homeotherm temperature regulation with inputs from peripheral skin receptors as well as core temperature. Previous neurophysiological experimentation by Hensel[26,27] and Zotterman proved the existence of cold and warm peripheral thermoreceptors and of the nervous transmission of this thermal sensory input into the central nervous system via the lateral spinothalamic tracts. This work also demonstrated that the individual thermal sensors in the skin showed a marked rise in impulses per second at a specific temperature range. The sum total of the thermal sensors covers the normal ambient range. The only interrelation between peripheral and central thermal inputs in the Davis study is that if core temperatures are widely variant from a normal range, a central mechanism overrides any peripheral input to the system. No quantified relationship between central and peripheral factors in temperature regulation were hazarded.

Yet the very existence of any interrelationship between central and peripheral temperature sensors in the homeotherm temperature regulatory system was itself challenged in the same year by Benziger.[2] In a study which has become known as the "ice cream experiment", Benziger flatly refuted the existence of any peripheral skin input into a temperature regulatory schema pointing out the fact that if an organ (skin) is both sensor and effector, its effector activity will interfere with its sensory ability. A naked male subject in a constant temperature hot room at 45°C was monitored for skin temperature, internal core temperature, and thermoregulatory response as measured by sweat evaporation. At intervals, the subject ate a large quantity of an ice water emulsion; changes in the above parameters were correlated with the internal chilling secondary to

the ingestion (See Figure # 1). Benziger's description of the experimental findings are as follows:

> "the curve for rate of sweating reproduces like an image, the internal cranial temperature. It seems difficult to avoid the conclusion, that internal temperature was the stimulus, and sudomotor activity was the response...it became obvious from these observations that both sudomotor and vasomotor activities responded to internal, not cutaneous, thermoception. ... it thus became improbable... that the thermoreceptors of the skin participate at all in human physical heat regulation by sudomotor and vasomotor activity."

Benziger goes on to state in his 'Results' section of the same experiment:

> "(1) the mechanism underlying human physical heat regulation has been described as a response to internal temperature by vasomotor and sudomotor action; (2) the absence of a contribution by skin temperature - and therefore by afferent impulses from cutaneous thermoreceptors - to the autonomic mechanism of human physical heat regulation has been demonstrated".

Benziger's startling hypothesis has found few adherents. Thermal comfort studies in various ambient temperatures had long since been published.[50,51] The subjective appreciations of thermal comfort "are closely correlated with skin temperature and, in hot environments, are even more closely correlated with sweat secretion",[51] and as has been later pointed out, thermal comfort perceptions actually " 'lead' the body temperature changes and are thus 'anticipatory' ".[11] This same study goes on to con-

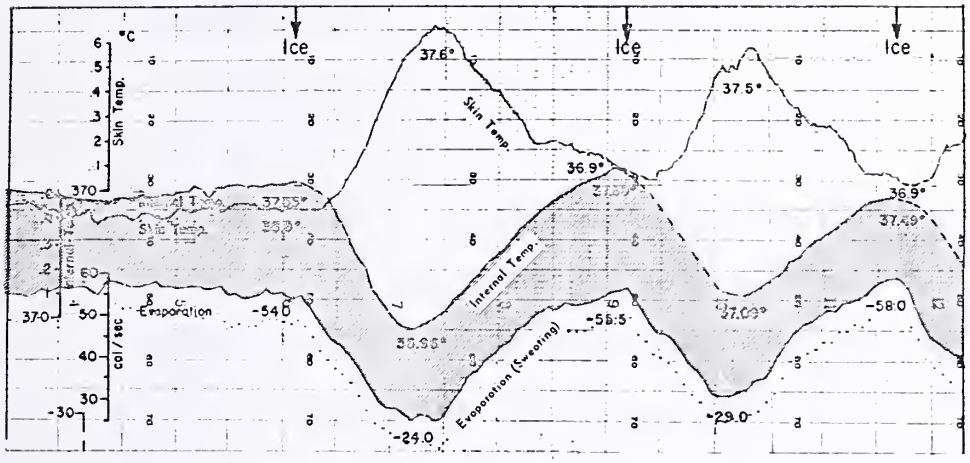


FIG. 1.—Effects of periodic changes of internal temperature, indueed by repeated oral ingestion of ice in hot environment (+45°C.) The effeets upon rate of sweating and skin temperature were simultaneously reeorded. For identification the area between the lines for internal temperature (upper line) and rate of sweating (lower line) has been shaded.

Figure 1

Benziger "ice cream experiment". 2 Sudomotor activity as a seeming function of internal temperature.

clude:

> "Finally, as in pain, discomfort is a stimulus par excellence for behavioral activity by man. Our data indicate that temperature signals from the various body structures furnish such stimuli whenever body temperatures are displaced from their physiological neutral levels. On the other hand, the displacement of body temperatures towards the physiological neutral level is associated with feelings of comfort even though these same temperatures previously caused discomfort. Thus thermal comfort, as a sensation, gives man both an anticipatory and early motivating drive for conscious action to effect a necessary change in his body's microclimate. Indeed, it seems plausible that behavioral activity stimulated by discomfort provides man with his principal means of long-term thermoregulation rather than the use of his natural but short-term means of thermal protection--sweating, vasodilation, vasoconstriction and shivering."

New physiological data already presented on warm and cold cutaneous receptors coupled with thermal comfort studies make Benziger's theory of temperature regulation seem highly improbable. In addition, Benziger's data, though impressive, has been duplicated using a computer model and multiple inputs. Hardy,[20] using a multiplicative input of core and skin temperatures into a computer model to produce calculated changes in muscle and skin blood flows, evaporative heat loss, and shivering, concludes:

> "the experimental data are explained well within the experimental error of the physiological measurements.

> In this connection, it might be pointed out that Benziger's conclusion, although apparently correct for explaining his "ice-cream experiment", are incompatible with a large body of data on the physiological responses to thermal transients. The above example seems to indicate that the interplay between central and peripheral temperatures is far too complex to permit desirable insight into physiological thermoregulation with simple intuition alone. One can only hope that aids to intuition such as computor solutions of network problems will be adequate".

Physiological research on the temperature regulating centers has thus localized the hypothalamus as the primary temperature regulating center and has elucidated certain of the input and output factors of the system.

> "There appear to be 2 principal factors which affect the functioning of the thermoregulatory centers. These are (1) the temperature of the blood perfusing these areas, and (2) incoming impulses from the peripheral thermoreceptors. Fear, excitement, and other emotions have also been shown to have minor effects upon the temperature-regulating centers. The presence of thermal detectors in the hypothalamus itself constitutes a central monitoring station for deep-body temperature, whereas the peripheral detectors may be regarded as warning devices which inform the thermoregulatory centers of changes in environmental conditions which will affect the exchange of

heat energy between the body and its surroundings."[36]

A more difficult problem is to further define the nature of the thermostatic controller unit within the hypothalamus. Despite the obvious difficulties in such work, progress has been made. The application of certain engineering concepts to a physiological regulating system has proven to be most helpful in unraveling some of the mysteries of the homeotherm thermostat.

To systematize the hypothalamic thermostat, there must exist input and output relations and a flow of information within a circuit. An automatic control system such as the homeotherm temperature regulatory mechanism needs some form of a closed loop, negative feed back arrangement. The controlling unit needs data from the controlled unit; in terms of temperature control, the hypothalamic thermostat needs data input (temperatures) from the body. Benziger would say that such input comes solely from the hypothalamus; the predominating opinions state that this input data is both from the hypothalamus, the skin and possibly other sites, e.g., muscle and spinal cord. The controlling unit needs one other crucial data input if it is to act as a controller - a reference or set point must come from a subsystem of the circuit, independent of the controlling system. The independence of this set point subsystem is vital. The subsystem must not respond to the same variables or in the same manner to the same variables as does the controlling system. The controller will then make a net resultant between the temperature of the controlled system and the independent reference set point and formulate an effector response. Effector responses may be relayed via neural and/or endocrine pathways; the end product will be heat loss or heat gain. This application of systems analysis to homeotherm temperature regulation is summarized by Hardy:[52]

> "physiological temperature regulator...the temperature insensitive neurons of the thermoregulating system that furnish the continuing input signal to the controller itself so that this signal may be compared with other signals from temperature receptors and adjustments made to minimize the deviation of the actual body temperature from its set point."

Taking this analysis one step further, physiological experiments can be designed to focus upon single biological components of the engineering system. For example, neurophysiological work on cutaneous warm and cold receptors and thermal comfort studies, are strong evidence for a feedback loop from one portion of the controlled system (skin) to the controlling system (hypothalamic thermostat). Shivering, sweating, and cutaneous hyperemia are examples of thermoregulatory responses of the controlled system to changes in core and/or skin temperatures. A large "black box" component, however, remains. The nature of the controlling system and its independent set point reference subsystem have been the object of experimental research during the past decade; the black box has begun to yield a portion of its contents.

A simplified block diagram of the homeotherm thermoregulatory system is shown in Figure # 2. Its major purpose is to systematize thinking in order to proceed experimentally to fill in specific inputs and outputs. The set point of reference temperature subsystem has its own input which may or may not include controlled system temperatures but which does include nonthermal variables. The set point of the controlling system may or may not be a fixed reference temperature; the simple thermostat comparison may, therefore, be an inadequate analogy. Thermoregulatory responses of the

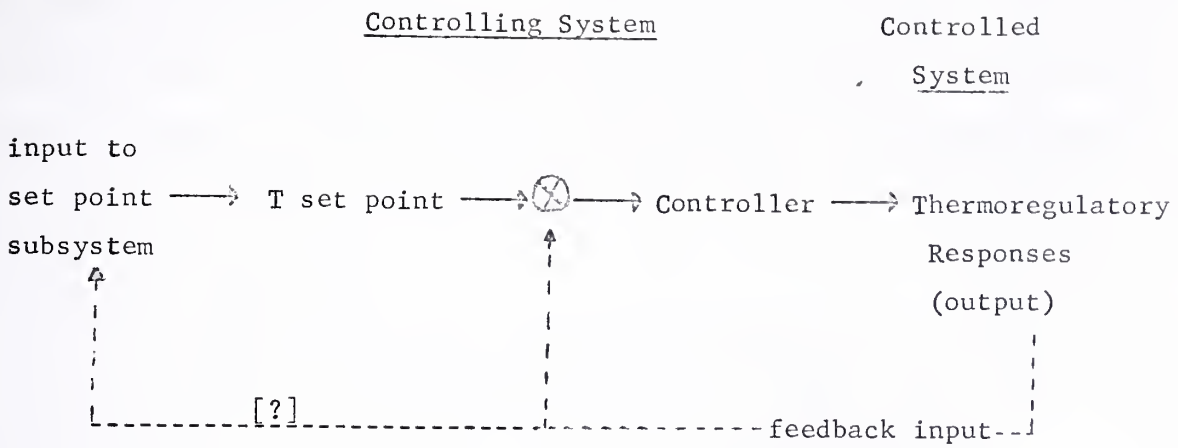


FIGURE # 2

Working Model of Homeotherm Thermoregulatory System.

controlled system may be observed and quantified. And finally, the question arises as to the nature of the feedback from the controlled system to the controller and to its location of re-entry into the circut.

It has been shown that non-thermal variables may alter body temperature. The menstrual cycle with its associated dip and then rise in basal body temperature at ovulation and its elevated body temperature during the progestational phase is a common example of a non-thermal variable (hormonal) influencing body temperature.[19] Temperature elevations are of course seen in fevers; bacterial endotoxins, endogenous pyrogen, and, more rarely, etiocholanolone have been implicated in the pathogenesis of certain fevers. All of these non-thermal variables seem to enter the thermoregulatory system by causing a quantitative adjustment of the set point. The newly changed set point causes the controller to affect mechanisms in the controlled system to conserve or dissipate heat. An experimental example of this effect is afforded by Andersen, et. al.[1] who injected a pseudo-

monas-derived pyrogen into dogs while controlling hypothalamic temperature directly by radio frequency stimulated implanted thermodes. Raising hypothalamic temperature immediately after administration of pyrogen blocked the development of the normal febrile response; cooling the hypothalamus resulted in a 'hyperfever'.

> "it seems probable that the pyrogen administered acts on the physiological thermostat directly. Hence, while this area is locally heated, the induced temperature change satisfies the requirements of the thermostat and prevents general fever development. Furthermore, the hyperfever produced by moderate, local cooling, shows the additive effect of two stresses working in the same direction, and it is quite conceivable that both stimuli are exerting their effect through the thermosensitive structures in the anterior hypothalamus."

The issue of whether thermal variables per se influence the set point is more difficult to prove. H. T. Hammel argues forcefully for this thesis - his work will be presented later. May it presently suffice that this issue is still open to question. Thus one component of the block diagram is, at least, in part understood. The subsystem for reference set point can be shown to respond to variables other than the temperature of the controlled unit, thereby making it a subsystem independent of the controlling system.

The block diagram of Figure # 2 does not describe anatomy. The anterior hypothalamus is known to include the "temperature regulation center", but prior to 1960 little was known as to the nature of such center(s). From the engineering standpoint, units (neurons) in the anterior hypothala-

mus must be responsive to the controlled variable (temperature) for the "temperature regulation center" to act as a controller. And, too, if a reference set point subsystem is located in the anterior hypothalamus, it must respond to the controlled variable in a completely different manner than do other neurons in the "center" if the subsystem is to be independent of the controlling system. If all neurons in the "temperature regulation center" are sensitive to temperature in the same manner, then the reference set point subsystem cannot be in the same anatomical locale.

The first work, as has much of the succeeding, to translate these engineering concepts to specific homeotherm mechanisms came from scientists at the John B. Pierce Foundation. Using thermodes to heat and cool the preoptic region of the anesthetized (urethane-chloralose) cat and a similarly implanted thermistor to monitor temperature, Nakayama, et. al.[33] were able to show specific and individual activity with local temperature changes (see Figure # 3). By local heating of the anterior hypothalamus, specific neurons were seen as rapid transducers of temperature. Thermoregulatory effector response was triggered -- respiration rate increased with hypothalamic heating. There was, too, a lag time between unit activity in the preoptic region with local heating and effector response. Neuronal adaptation to temperature was not found; temperature sensitive neurons in the cat hypothalamus maintained a constant firing rate as long as temperature was held constant.

The proof of the existence of warm sensitive neurons in the cat hypothalamus provides one functional unit to the controlling system. Yet the bulk (80%) of the neurons studied in the area of the "temperature regulation center" were insensitive to local temperature changes.[20] To ascribe a function in the temperature regulatory scheme to these temperature insen-

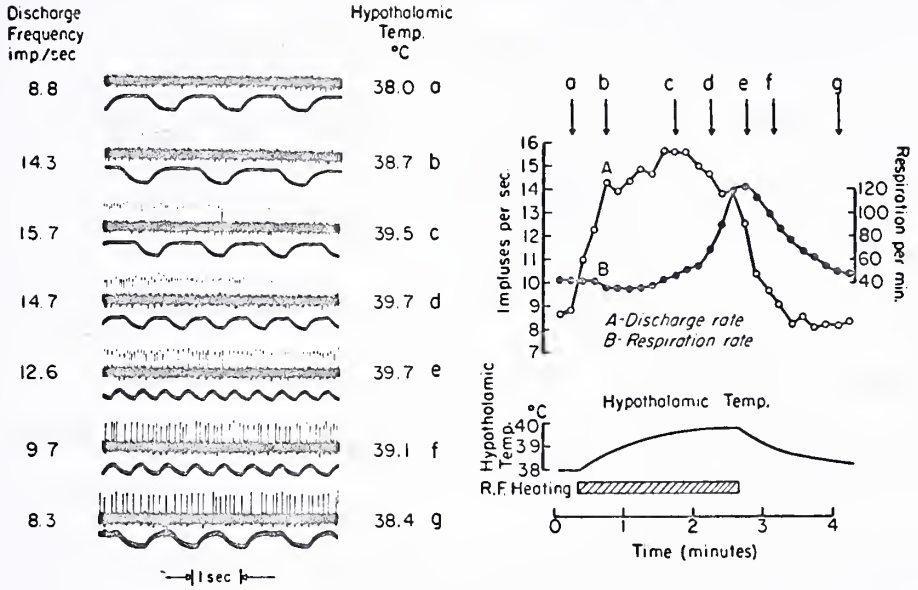


Fig. 8. At left: Firing rate of neuron in the hypothalamus at various temperatures. At right: Time sequence af changes in neuronal firing rate, respiration rate and local tissue temperature during a 2 1/2 minute period of radio frequency heating.

Figure 3

Neuronal activity in the anterior hypothalamus in response to direct local heating. (33)

sitive neurons in the anterior hypothalamus would be but informed speculation. Applying the engineering systems model once again, as well as the anatomical proximity to temperature sensitive neurons, Hardy hypothesized a potential set point function for these temperature insensitive neurons. The existence and function of such neurons, if in fact part of a reference set point system, could be predicted by the theory behind the controller unit; that is, set point neurons respond differently to the controlled variable than do temperature sensitive neurons. It is indeed an attractive speculation.

Two other experimental findings are insightful into the workings of the controller system. Taking the experimental model as described in the cat to the dog, Hardy, et. al.,[23] duplicated the finding of heat sensitive and temperature insensitive neurons in the anterior hypothalamus, thus extending the concepts to a new species. Cold sensitive neurons were also demonstrated - neurons which responded to cooling with increased impulse rates.

Combining this experimental data into a hypothetical plan for a controlling system, though in some respects speculative, is a useful aid to thinking. Warm and cold sensitive neurons in the anterior hypothalamus act as sensors to core temperature. Temperature insensitive neurons may play a role in the reference point subsystem. Comparison could be made by the controller between set point reference and actual core temperature and an effector response generated. Experimental data compatible with such a model comes from many sources including Hammel, et. al..[18] By implanting needle thermodes in the anterior hypothalamus of unanesthetized dogs, hypothalamic temperature could be varied and thermoregulatory effector response monitored. Cooling the hypothalamus resulted in vasoconstriction and shivering; warm-

ing the hypothalamus stimulated heat dissipatory mechanisms. Such data does not prove the reference set point function of temperature insensitive hypothalamic neurons, nor does it evaluate the complete physiologic feedback loop, but it does point toward the workings of the homeotherm thermostat.

As previously described, thermal inputs from both core and periphery are integrated, presumably at the level of the hypothalamus, and are multiplicative in driving the thermoregulatory apparatus. To study the relative importance of central and peripheral factors in homeotherm temperature regulation, Fusco, et. al.,[10] using unanesthetized dogs, locally varied hypothalamic temperature in different ambient temperatures and measured thermoregulatory response. A neutral ambient temperature (26°C) provided a baseline; at this temperature only a central drive to thermoregulation existed during the phases of local hypothalamic heating and recovery. Dogs at neutral ambient temperature responded to hypothalamic heating by affecting a 30-40% reduction in rate of heat production, which, in turn, caused rectal temperature to fall 0.8 - 1.0°C. Once hypothalamic heating ceased, the dogs raised the depressed core temperatures back toward normal levels by increasing metabolic rate. Again, this heat gaining drive in neutral ambient conditions is central in origin. By changing the ambient temperatures, any peripheral drives to thermoregulation would be apparent as overlays upon this neutral ambient temperature baseline. Table # 1 shows the results of the study. Hypothalamic heating lowered core temperature nearly 1°C in all ambient conditions. The heat productions during and after hypothalamic heating in dogs at warm or cool ambient conditions are, therefore, measures of the interplay between central and peripheral input drives to thermoregulation. In the cool environment, resting baseline metabolism

	Neutral (26°C)	Warm (29°C)	Cool (14°C)
core temperature after hypothalamic heating (rectal temperature)	↓ 0.8°C-1.0°C	↓ 0.8°C-1.0°C	↓ 0.8°C-1.0°C
heat production during hypothalamic heating (compared to own baseline)	↓ 30-40% slight vasodilation	↑ evaporative heat loss x 5 marked vasodilation	↓ 10% no vasodilation
heat production after hypothalamic heating (compared to neutral ambient baseline)	1 (baseline)	35% less than baseline	30% more than baseline

Table # 1.

Interplay of Peripheral and Central Drives to Thermoregulation.

Date from Fusco, et.al.[10]

before hypothalamic heating was 40% higher than resting metabolism at neutral ambient conditions. During hypothalamic heating, heat production in dogs at 14°C fell but 10% from baseline values, while heat production in dogs kept at 26°C fell 30-40%. "This difference in response was due to a peripheral 'cold' drive which effected and maintained an elevation in heat production, and opposed the central drive. Thus, instead of a reduction in metabolic rate to 30-40% of the resting level, which occurred in the neutral environment, the central heating was effective in lowering metabolic rate only a small amount - approximately 10%".

The interrelationship between skin temperatures and core temperatures

to affect a thermoregulatory response again implies a set point reference around which the controlled system must fluctuate. Non-thermal variables may affect the controlling unit set point (pyrogens and hormones for example) as has been demonstrated, but an assumption has been made that any given input combination of skin and core temperatures will elicit a unique thermoregulatory response. To further quantify the interrelationship between thermal input and effector output, Hammel, et.al.[19] monitored and varied core, skin, and ambient temperatures while measuring metabolic rate in unanesthetized dogs and monkeys. With this model, Hammel could elicit shivering in an animal in a cold environment with the same or higher hypothalamic temperature as the same animal resting in a neutral environment, as well as elicit panting in an animal in a hot environment with a hypothalamic temperature equal to or lower than the same animal in a neutral environment. The effects of sleep on body thermoregulation were also evaluated and may be summarized as:

1. at the onset of sleep, the hypothalamic temperature falls, but the rate of heat loss increases.
2. during sleep, hypothalamic temperature is 1-2°C lower than while awake.
3. thermoregulatory responses are similar awake and asleep.
4. upon awakening, the hypothalamic temperature rises, but the rate of heat loss decreases from sleep-time values.

Hammel interprets this data in a provocative, though as yet unproven, manner. He suggests that the set point is adjustable and responds to the aforementioned conditions as follows:

Set Point	Stimulus
	rising or elevated skin and non-hypothalamic internal temperatures
decreased	
	entering sleep
	during sleep
---	---
	falling or lowered skin and non-hypothalamic + internal temperatures
increased	
	awakening

In his discussion, Hammel points out that experiments which vary hypothalamic temperature directly via implanted thermodes may prove that temperature regulatory responses can thus be elicited (in fact, Hammel's own data shows that a 1°C drop in hypothalamic temperature elicits a four-fold increase in rate of heat production), but that such a model is not physiologic. Animals placed in cold or hot ambients affect homeostatic responses with little change in hypothalamic temperature. Hammel states:

> "Thus, an adequate description of the central temperature controller must account for its sensitivity and responsiveness to physiological or experimental displacements in its own temperature. At the same time such a description must account for a response of the central controller to external thermal stress, when there is no change in its own temperature and, finally, the description must allow for a response which is the reverse of the normal response during the transition from wakefulness to sleep or vice versa, and for normal responses during wakefulness and sleep even though the temperature of the central controller during sleep

may be as much as 2°C lower than in wakefulness."

By envisioning a set point adjustable to such variables as thermal ambients, skin and core temperatures, and state of wakefulness, the homeotherm thermal regulatory controller unit would be able to function at the same gain level at all times and not be dependent under normal circumstances on an actual change in hypothalamic temperature to trigger a significant thermoregulatory response.

Heretofore, most of the literature review has concerned itself with animal models and extensive central nervous system manipulations upon such creatures. Much basic scientific information has become available through such study, particularly about neuronal activity in the hypothalamic temperature regulatory centers. Human experimentation in this field has corroborated animal work in terms of input-output analyses in heat balance studies, and, as for example in the Benziger work previously cited, has indirectly pointed toward models of homeotherm thermoregulation. The difficulties in direct human experimentation in this field are manifestly obvious. One human model, however, which has proven to be insightful has been the chronic spinal man.

Downey, et.al.,[6] using high cervical cord transection tetraplegics has verified the existence in man of central nervous system effector(s) which respond to the cooling of its blood supply. Cooling the paralyzed insentient portion of a cervical cord transection patient results in increased metabolism and a shivering response in the innervated musculature when central temperature as measured by tympanic membrane thermocouple falls to approximately 35.6°C even though skin in the sentient body portion is kept above 34°C. Downey states that this is evidence for "deep temperature sensitive structures that could initiate shivering without a

cold stimulus from the sentient skin".

Extending this study to patients with thoracic cord transections (T-2 to T-11), Downey, et.al.,[7] by varying ambient temperatures as well as the temperature of the insentient body portion by the use of a surgical cooling blanket, provides further evidence for the interrelationship between skin sensor input and central temperature sensors to affect a thermoregulatory response. Downey's data may be examined as follows:

I. Cooling insentient body wile maintaining sentient body temperature above 35°C.

Central temperature as measured at the tympanic membrane decreases to 35.6°C - 35.8°C without central thermoregulatory response (shiver or increased oxygen consumption). Below this central temperature, oxygen consumption increases (up to 60% above basal) and shivering in innervated (sentient) body occurs causing central temperature to level and then rise.

II. Cooling insentient body while allowing sentient body temperature to fall below 34°C [ambient temperatures of 22 - 24°C].

Central temperature decreases in these studies and triggers central thermoregulatory responses at higher core temperatures than in the studies performed at higher ambient temperatures.

These comparisons were made with the same subjects under the two conditions. Interpatient comparisons demonstrate a response gradient to decreases in central temperature varying with cord transection level as:

Cord Level	Temperature Ear at Thermoregulatory Response In Warm Ambient	Temperature Ear at Thermoregulatory Response In Cold Ambient
T_2	35.5°C	35.6
T_{10}	35.8	36.4

In his discussion Downey concludes:

1. paraplegic and tetraplegic patients respond similarly to central cooling when sentient skin is not cooled--both study groups affect central thermoregulatory responses at core temperatures approximating 35.6° - 35.8°C.
2. Lower cord lesion patients affect thermoregulatory responses at higher central temperatures than do high spinal patients when sentient skin is cooled.

"It would appear that when little skin cooling can occur as in the high spinal patients, thermoregulation in the cold is dependent largely on deep or central temperature receptors and that these respond and initiate increased heat production only when a rather great fall in temperature has occurred. When patients with the greater areas of sentient skin are exposed to central and skin cooling there is an apparent upward shift of the internal

temperature at which increased heat production occurs".

Downey's experiments with the chronic spinal man model support the concept of both central and peripheral skin sensory inputs contributing to affect a thermoregulatory response. A similar model, utilizing however healthy individuals with completely intact thermoregulatory mechanisms is a patient under spinal anesthesia. This model is an acute preparation which may temporarily alter the thermoregulatory input and response characteristics, and which, upon the cessation of the effects of the anesthesia, should once again allow the subject to utilize a completely intact thermoregulatory apparatus to achieve thermal homeostasis.

Spinal Anesthesia

Spinal anesthesia is now over seventy years old as a clinical means of providing anesthesia.[8] The instillation of local anesthetic in the lumbar subarachnoid space creates firstly a sympathetic blockade and then, if adequate quantities of anesthetic are employed, sensory and motor paralysis covering a variable portion of the body. Merely to gloss over these profound effects of spinal anesthesia without discussing the physiology of the state of the anesthesia would preclude the understanding of why spinal anesthesia is a model useful in temperature regulation studies.

The primary physiologic effect of spinal anesthesia is not sensory and motor paralysis of the lower portion of the body, despite its obvious clinical importance. The preganglionic sympathetic fiber paralysis caused by spinal anesthesia, acting predominantly at the nerve root level, is its major and primary physiologic effect.[14] Nearly all of the associated physiologic changes under spinal anesthesia can be accounted for by this sympathetic blockade.

Once the local anesthetic agent has been instilled in the lumbar subarachnoid space, the nerve fibers traversing the subarachnoid space become paralyzed according to the effective concentration of the anesthetic and the size of the nerve fiber.[14] Unmyelinated and thinly myelinated nerve fibers are first to be affected--this fact coupled with the high ratio of post-ganglionic sympathetic synapses subsequently blockaded account for the rapid and widespread sympathetic autonomic blockade. Sensory anesthesia for temperature, pain, and touch ensues, followed by motor and finally proprioceptive paralysis if adequate quantities of anesthetic are employed.

These effects can be observed in the operating room soon after the induction of spinal anesthesia. The patient will firstnote an increased feeling of warmth in his lower extremities--the perceived sensory input

which describes an increase in cutaneous blood flow--as sympathetic blockade begins. It is well known that normal arteries and arterioles dilate with sympathetic denervation,[14] hence more blood is delivered to the skin. Next pinprick sensation is lost, providing the anesthesiologist with a functional tool in determining the level of the spinal anesthesia. Motor and proprioceptive capability are the last to disappear.

An important point must be raised concerning the anatomic level of spinal anesthesia. Greene[13] points out the zone of differential blockade in spinal anesthesia. He compared the anatomic level of anesthesia by pinprick sensation (e.g., pain afferents) with the ability to perceive cold. Nerve fibers transmitting afferent impulses from skin cold receptors are but slightly larger than preganglionic sympathetic fibers, and thus will be paralyzed by local anesthetics much as thoracolumbar sympathetic outflow. The results of this comparison are not trivial. A two spinal segment difference between cold sensation loss versus pinprick sensation loss was an average finding. Loss of cold sensation was always anatomically higher than the pinsensation level. One patient described in the study had an anatomical differential blockade of six spinal segments. Thus one can clearly see that the level of spinal anesthesia determined by loss of pinprick sensation does not include the full upper range of sympathetic denervation. This zone of differential blockade under spinal anesthesia is clinically important, in that the entire thoracolumbar sympathetic outflow may be paralyzed with its attendant effects (see later) without complete thoracic sensory anesthesia.

Since sympathetic denervation is the physiologically crucial aspect of spinal anesthesia, it is well to examine its effects. This can best be

accomplished by studying the cardiovascular response to spinal anesthesia.

The "effects of spinal anesthesia on the cardiovascular system are the results of preganglionic sympathetic blockade" and not the direct effects of local anesthetics in the blood stream. The height of the spinal blockade (i.e., sympathetic denervation) determines the cardiovascular response. The effects on specific organs is predominantly due to the changes in blood flow to that organ.[14] Arterial and arteriolar dilatation as a vascular response to sympathetic denervation has been noted, and a rule of thumb can be made by stating that no arteries or arterioles constrict when sympathetic tone is lost. There is, however, a variable quantity of vasodilation of blood vessels per each specific organ system. Vasodilation with its resulting increased blood flow is most noted in the skin and subcutaneous tissues, least in the splanchnic bed, and intermediate in the muscle mass.[14] A rough measure of vasodilation--the total peripheral vascular resistance (calculated as:

$$\frac{\text{mean aortic pressure (mm hg.)}}{\text{cardiac output (cc per sec.)}} \times 1332$$

shows a decrease with spinal anesthesia and correlates well with the degree of sympathetic blockade.[14]

The relative cutaneous hyperemia secondary to sympathetic blockade makes the insentient skin a heat losing organ. Using needle thermistors to measure muscle and subcutaneous tissue temperatures in the insentient body region, Smith[48] notes a rise in peripheral temperatures--scientific corroboration of the subjective feeling of skin warmth noted by patients upon receiving spinal anesthesia. This cutaneous hyperemia--heat losing phenomenon is best explained by studies of the microcirculation.

With sympathetic blockade, muscle tone in meta-arterioles and precapil-

lary sphincters is reduced, but not entirely abolished. Further reduction in vascular muscle tone can be achieved by vaso-active compounds such as histamine. This reduction in vascular tone secondary to sympathetic blockade is, as stated previously, greatest in skin and subcutaneous blood vessels. Sympathetic blockade also affects venous dilation, but due to the small quantity of vasomotor smooth muscle investing venules and small veins, venodilation is nearly maximal. The entire post-arteriolar circulation becomes engorged with blood; greater numbers of capillaries at any one moment are filled with blood than under normal conditions. The net result of these vascular changes is that a greater than normal quantity of blood is in the periphery of the circulatory system.[14]

Hypotension with its feared sequelae of impaired perfusion to vital organs obviously lurks as a potential danger with spinal anesthesia. With an increased quantity of blood in the peripheral circulation, venous return to the heart becomes precarious. A simple positional maneuver such as a slight reverse Trendelenburg may further reduce venous return to the heart, decrease cardiac output, and precipitate systemic hypotension.[14]

If significant systemic hypotension does not develop and if vasopressors are not employed to raise peripheral vascular resistance, studies can be made on blood flow to body regions within and outside of the range of sympathetic blockade. It must be re-emphasized that all such studies are worthless if systemic blood pressure is not maintained and/or if sympathicomimetic drugs are not screened from the study.

Two such papers are of interest.[42,43] In subjects receiving spinal anesthesia but not undergoing surgery[42] comparisons of blood flow rate and volume in the upper and lower extremities during "high" and "low" spinal anesthesia were performed. Systemic blood pressure was maintained by

intravenous fluids alone. "Low" spinal anesthesia was taken as below T-4 (sensory loss to pinprick at nipples; no increased warm cutaneous sensation in upper extremity); "high" spinal anesthesia as including the upper extremity within the field of sympathetic blockade. The units quantifying blood flow rate and volume relate to the plethysmographic equipment utilized in the study--it is the raw numerical data which is of greatest concern.

I. High Spinal Anesthesia--above T-4 ("release vasomotor tone in fingers")

1) increased rate of circulation in fingers and toes

2) finger blood flow (cc/10cc of part/minute)

- before spinal -- 0.32
- after spinal -- 1.11

II. Low Spinal Anesthesia--below T-4

1) increased rate of circulation in toes decreased rate of circulation in fingers

2) finger blood flow (cc/10cc of part/minute)

- before spinal -- 1.28
- after spinal -- 0.50

3) Toe blood volume compared to finger blood volume (cc/10cc of part)

	Before Spinal	After Spinal
Toe	.0018	.0052
Finger	.0065	.0025

Similar results were obtained in patients receiving high and low spinal anesthesia and undergoing surgery.[43]

These two studies effectively demonstrate the changes in cutaneous

blood flow between sentient and insentient portions of the cutaneous body under spinal anesthesia. If systemic hypotension were to develop, all blood flow rates and volumes would decrease drastically. Possible explanations for this differential in cutaneous blood flow between upper and lower extremity in patients undergoing low spinal anesthesia include:

(1) A decrease in actual blood volume during spinal anesthesia resulting in hypovolemia.

> This explanation, though attractive, is specious. If gravity is not employed to assist venous return to the heart during spinal anesthesia, peripheral pooling of blood may decrease the effective circulating blood volume by 50%.[14] But, by using Evans blue dye techniques, it is shown that the actual circulating blood volume during spinal anesthesia is relatively stable.[14] Proper patient management by position alone is often enough to insure adequate venous return and cardiac output.

(2) Barroreceptor activity causing sympathetic discharge to increase vasomotor tone in sentient body region.

> If systemic blood pressure should decrease, pressor receptors in the carotid sinus and aortic arch would, under normal conditions, trigger a sympathetic cardio-accelerator as well as a sympathetic vascular response to elevate systemic blood pressure. If both preganglionic cardio-accelerator and vasomotor sympathetic nerves are paralyzed (i.e., spinal sympathetic blockade at T-1),

this compensatory mechanism is impossible--"If the anesthetic reaches higher thoracic levels, the ratio is in favor of vasodilatation, and hypotension ensues. If the anesthetic remains at lower levels, a sufficient number of unblocked roots capable of transmitting compensatory constrictor impulses are left to prevent a major drop in arterial blood pressure."[30]

Low spinal anesthesia would, however, still allow this compensatory mechanism to respond to a drop in blood pressure. "At the same time that arterial and arteriolar dilatation occurs in sympathetic denervated areas, compensatory reflex vasoconstriction may take place in those parts where sympathetic nerve supply has remained unaffected. Such vasoconstriction is initiated by a fall in arterial blood pressure."[14]

If, however, blood pressure were not to fall while undergoing low spinal anesthesia, reflex vasoconstriction secondary to barroreceptor activity should not occur. Any vasoconstriction in the sentient body portion, in the face of adequately maintained arterial blood pressure, would be the result of mechanisms other than pressor reflex activity.

(3) In an effort to conserve heat, vasoconstriction occurs in the sentient portion of the body.

Smith, in a study quoted previously, also monitored rectal temperatures of patients undergoing low spinal

anesthesia. "In spinal anesthesia, there was invariably a drop in rectal temperatures and a rise in peripheral (e.g., insentient) temperatures."[48] The heat loss by the body secondary to sympathetic blockade and its resulting cutaneous hyperemia is maximal when the systemic blood pressure is maintained.[9] Patients are "less able to maintain constant body temperatures... with sympathetic blockade."[14]

To evaluate the causes for upper extremity vasoconstriction in patients undergoing low spinal anesthesia, it is, therfore, necessary to hold systemic blood pressure at, or close to, normotensive values. Once this is accomplished, the role of temperature regulatory mechanisms in spinal anesthesia can be ascertained.

An experimental model using spinal anesthesia to acutely, but only partially, disrupt normal thermoregulatory mechanisms has been suggested; a review of much of the recent literature on homeotherm temperature regulation as background material has also been presented. This current study is undertaken to evaluate the thermoregulatory response of patients undergoing spinal anesthesia.

Methods

Cases for this study were selected using the following criteria:

1. male or female between the ages of 18-40 years
2. admitted to Yale-New Haven Hospital for elective operations for which spinal anesthesia was the anesthesia of choice as determined by the department of anesthesia
3. normal hematocrit, electrocardiogram, blood pressure
4. scheduled operating time less than 90 minutes; no operations within the peritoneal cavity
5. patients on no prior medications save birth control pills (case #3)

On the evening prior to surgery, patients volunteering for this study (see Appendix for consent form) are measured for height and weight, and surface areas are calculated using a standard monogram. Standard preoperative preparations per each case are followed. On the morning of surgery, patients are premedicated with seconal or atropine and seconal and brought to an empty operating room 90 minutes prior to surgery. The Brookline Temperature Computor is attached (see Appendix for photographs) to the patient to measure temperatures of the forehead, arm, hand, chest, abdomen, thigh, calf, foot, core (rectal) and ambient environment (wall). Surface temperature probes are attached to skin by a thin strip of adhesive tape which does not cover the entire probe, thus allowing for physiologic insensible water loss (with resulting skin cooling) from the immediately adjacent skin. A drop of collodion between skin and probe seals the attachment. Collodion does not alter thermistor readings of skin temperature ($\pm$ 0.05°C).

The Brookline Temperature (BTC) - Beaver prototype is an analog computor designed to provide temperature and heat flow measurements from a

surface to the ambient environment. Temperatures from eight pre-selected body locations (see Appendix) as well as ambient environment are obtained from the BTC Yellow Springs Instruments thermilinear probes (#44202) and are utilized to calculate a weighted skin temperature according to the formula:

$$T \text{ mean skin} = \frac{T_1 W_1 + T_2 W_2 + \ldots + T_8 W_8}{W_1 + W_2 + \ldots + W_8}$$

where $T_1 - T_8$ are individual skin temperatures

$W_1 - W_8$ are individual weighting factors (values from 1-9)

Weighting factors are determined by the percentage of body surface area represented by each temperature probe; weighting factor values do not alter probe temperature readings.

The BTC automatically calculates heat flow in Kcal./hr. by the Stefan-Boltzman equation for radiative heat loss:

Heat Flow = Q = HA [T skin mean - T ambient]

H = heat transfer coefficient = 4.4 [entered as gain #2]

A = effective radiating body surface area [entered as 60% total surface area as gain #1]

Rectal temperatures are obtained by a separate Brookline Instruments Thermometer calibrated against a U. S. Bureau of Standards Thermometer to $\pm$ 0.1 °C. BTC thermilinear probes were calibrated against the U. S. Bureau Standards Thermometer to $\pm$ 0.2°C.

Mean body temperatures are calculated as:

$$T \text{ mean body} = .25 \ (T \text{ mean skin}) + .75 \ (T \text{ rectal})$$

Patients are allowed to lie supine, awake, as naked as possible, and free to move extremities for a 40 minute equilibration period prior to administration of spinal anesthesia. Temperature recordings and comfort indices are taken at 10 minute intervals prior to anesthesia. Comfort indices are subjective cerebral appreciations of thermal change and gradients throughout the body. Patients are asked to compare body locations as to temperature, and are asked about total body comfort (i.e., hot, warm, cool, cold).

After the administration of spinal anesthesia (pontocaine with epinephrine or pontocaine alone), temperature readings, comfort indices, levels of anesthesia to pinprick and cold discrimination [ether soaked gauze lightly applied to skin] and blood pressure are measured at five minute intervals for at least 30 minutes prior to operation. During the time of operation and post-operatively in the recovery room annex, these parameters are measured at 15 minute intervals until 30 minutes after sensory discrimination to pin and cold is intact.

Blood pressures were maintained by intravenous fluids and atropine - no vasopressors were utilized in any case. At no time during the experimental period were subjects unresponsive to verbal commands or questions.

Results

The four subjects studied exhibited decreases in post-operative core temperature which ranged from 0.6°C to 2.6°C. These temperature changes were analyzed in relation to age, sex, surface area, duration of operative procedure, operating room temperature, and anatomic level of spinal anesthesia. No significant correlations were demonstrated between decrease in core temperature and any of the aforementioned variables save for anatomic level of spinal anesthesia (Table 1). Case #1 was the only case in which the spinal anesthesia level was below T_6 (i.e., a "low spinal"); the post-operative hypothermia of case #1 was profoundly less than that of cases #2, 3, and 4.

As the effects of spinal anesthesia wane, as measured by anatomically receeding pin and cold sensation tests, proprioceptive and motor capabilities are first to be regained in the lower limb as a function of large nerve fiber size. No correlation existed between exact sensory levels of anesthesia and the reestablishment of motor function. A specific correlation did exist between sensory level of spinal anesthesia and the reacquisition of vasomotor activity in the lower limb. All patients began to regain vasomotor tone in the foot (as defined by a decrease in foot skin temperature of greater than 1°C in 15 minutes) at comparable spinal sensory levels appreciably above the lumbar sympathetic outflow (Table #2).

Cerebral perception of skin temperature change as compared to actual skin temperature change was analyzed in all subjects studied. Post-operative decrease in foot temperature, as a result of the re-establishment of vasomotor tone, at a rate of greater than 1°C in 15 minutes was used as an objective index of temperature change. Subjective response indicating that the feet, previously insentient to cerebral perception, first felt "cool" to the subject was taken as the initial higher cortical appreciation of

Case	Age	Sex	Surface Area	Op. Length	O. Temp.	Fall in Rectal Temp.	Level Anesthesia pin/cold	Operation
#1-E.S.	20	male	$1.97m^2$	45 min.	21.8°C	0.6°C	T_6/ T_5	Circumcision
#2-G.B.	23	female	$1.71m^2$	60 min.	21.7°C	1.4°C	T_3/ T_3	A-P repair
#3-J.G.	32	female	$1.68m^2$	45 min.	21.2°C	2.6°C	T_2/ T_2	Vaginal BTL
#4-H.A.	24	male	$1.86m^2$	60 min	21°	1.9°C	T_2/ T_2	Inguinal Hernia

Table # 1

Case	Maximal Level Spinal Anesthesia [pin/cold]	Level Anesthesia @ 1st motor function great toe - [pin]	Level Anesthesia @ cutaneous temperature decrease (>1°C/15 min) in foot [pin/cold]
I	T_6/ T_5	T_{11}	T_9/ T_7
II	T_3/ T_3	T_{12}	T_{10}/ T_9
III	T_2/ T_2	T_4	T_8/ T_7
IV	T_2/ T_2	T_5	T_{10}/ T_9

Relationship between the sensory level of spinal anesthesia and the reestablishment of motor and vasomotor function in the foot.

Table # 2

newly regained cutaneous cold sensory input. In 3 of the 4 cases studied, cerebral perception of temperature change preceeded the actual decrease in temperature. Further comparisons were made between cerebral perception of actual foot temperature (when the foot was judged to be the coldest part) and objective thermal data. Results of these thermal comfort studies are seen in Table # 3.

TABLE 3

Case	Spinal Level @ 1st perception feet are "cool"	Spinal Level @ decrease foot temperature > 1°C/15 min.	Spinal Level @ 1st perception foot coldest body part	Spinal Level @ Feet actual coldest body p. t
I	T_{11} (pin)*	T_9	S_1	T_{12}
II	T_5	T_{10}	L_5	NEVER- hands always colder than feet
III	T_6	T_8	L_1	S_1 (Temp. feet = T-hand $\pm$ 0.2°C
IV	T_8	T_{10}	T_{11}	L_5

* all spinal levels in this table are to pin sensation

Cerebral thermal perception of foot temperature compared to actual foot temperature as a function of sensory level of spinal anesthesia.

Discussion

The four subjects studied experienced substantial post-operative hypothermia--the net result of the imbalance, created by the spinal anesthesia, between heat production and heat loss. Certain variables were controlled so as not to affect the magnitude of the hypothermia, namely:

1. age: There is an inverse proportion between age and the ability to maintain a constant body temperature; elderly (above 60 years) patients undergoing operative procedures under general anesthesia are less capable of increasing heat output to balance increased heat losses than are their younger counterparts.[12] All patients in this study are within the age range of 20-32 years.

2. operation: Prolonged operative procedures and opening of the peritoneal cavity are both associated with increased heat losses.[12] All of the cases in this study were 60 minutes or less, and in none of the cases was the peritoneal cavity opened.

3. ambient temperature: all ambient temperatures were in the range of 20-23°C.

The initial control period, pre-spinal anesthesia, of exposure to ambient temperatures in the 20-22°C range, demonstrates the normal thermostatic mechanisms of healthy, young adults. Skin temperatures in all body areas decreased as a result of cutaneous vasoconstriction. This reduces radiative heat loss and contributes to the maintenance of a constant core temperature. Theoretically, in the face of increased radiative heat loss, increased heat production could maintain the core temperature constant, but no direct evidence of increased thermogenesis (i.e., shivering) was demonstrated at this time. During this equilibration period, the

intact peripheral thermoregulatory drive involving cutaneous cold receptors and central nervous system integration results in increased sympathetic tone in cutaneous blood vessels. The central thermoregulatory drive involving direct hypothalamic response (with resultant intense shivering and vasoconstriction in response to cold) to changes in the temperature of its blood supply is not triggered since core temperature is unchanged.

Spinal anesthesia partially interrupts these normal thermoregulatory reflexes. A model is thus produced with the following characteristics:

1. Hypothalamic central temperature sensor and thermoeffector apparatus is intact.
2. No cutaneous temperature data is available to the hypothalamus from all body parts below the level of spinal anesthesia.
3. Cutaneous and muscular thermoeffector responses below the level of spinal anesthesia are paralyzed due to sympathetic and motor neuron blockade.
4. Sympathetic blockade results in temporary vasodilation of cutaneous blood vessels in all areas affected by the spinal anesthesia, greatly increasing radiative heat loss.
5. Sentient body area not affected by the spinal anesthesia retains its sensory, muscular, and vasomotor capabilities.
6. Normal thermoregulatory mechanisms are regained as the spinal anesthesia wears off, thus allowing an increasingly intact thermoregulatory system to respond to a temporarily abnormal thermal stress.

Case #1 demonstrates the effects of a "low spinal" - i.e., much of the thoracic sympathetic outflow remains intact. The rapid thermal dissociation created by the spinal anesthesia of sentient and insentient body portions and the subsequent thermal course is demonstrated in Figure #4. Sympathetic blockade below T_5 causes increased radiative heat loss from the effected area. Compensatory vasoconstriction occurs promptly in the sentient body portion to minimize net body heat loss. Core temperature decreases slowly at a rate of 0.8°C/hr. to a value 0.6°C below baseline, and remains depressed for three hours post-operatively as the spinal anesthetic begins to wane. Vasomotor tone is regained in the insentient body portion hours before the reestablishment of cutaneous sensation, and a central thermoregulatory response (shivering) occurs only after the reestablishment of cutaneous sensory input from the heretofore insentient body portion. This centrally mediated shiver response occurs at a time when core temperature is not maximally depressed, and is, in fact, rising.

The thermal course of Case #1 demonstrates the integration of cutaneous sensory temperature data with core temperature data to affect a thermoregulatory response. The intact portion of the thoracic sympathetic outflow produced heat-retaining vasoconstriction in approximately 40% of the body surface area, thus keeping net body heat loss and, therefore, core hypothermia to a level which does not, in and of itself, elicit a centrally mediated metabolic response. It is only after peripheral cutaneous cold sensor input from the previously insentient body portion becomes available to the hypothalamus that a central response is triggered. No central metabolic response occurs when the core temperature is maximally depressed; only when the hypothalamus perceives near total body cutaneous cold sensor data in addition to relative core hypothermia is a central shiver response

CASE #1 (pt. E.S.)
#78-33-82
August 27, 1970

OPERATION
DRAPED

SPINAL LEVEL (PIN)

T_{10} T_6 T_6 T_7 T_8 T_{10} T_{11} T_{12} L_1 L_3 L_3 S_1 S_3

SHIVER

T_{RECTA}

$T_{MEAN\ SENTIEN}$

$T_{MEAN\ INSENTIEN}$

$T_{AMBIENT}$

O.R. #5 → O.R. #7 → RECOVERY ROOM

38° 37° 36° 35° 34° 33° 32° 31° 30° 29°

23° 22° 21° 20°

1 2 3 4 5 6 7 8 9 10

TIME - HOURS

Figure 4

elicited.

Cases 2, 3, and 4 demonstrate the thermal course of patients undergoing "high spinal" anesthesia - i.e., little thoracic sympathetic outflow remains intact as indicated by a rise in cutaneous temperature in the upper extremity. Only a small percentage of the cutaneous body remains sentient in high spinal anesthesia; as such, it is but a limited surface area which is capable of motor (shiver) and sympathetic (vasoconstriction) response to post-operative hypothermia. The thermal course of one such case is illustrated in Figure #5.

Directly upon the induction of spinal anesthesia, skin temperatures increase in the denervated areas secondary to sympathetic blockade. The innervated body portion vasoconstricts in an effort to minimize net heat loss. Forehead temperatures, the only single cutaneous temperature in a completely sentient zone in the high spinal anesthesia cases, decreased an average of 3.1°C compared to a decrease of 1.9°C in forehead temperature of Case #1. Despite this strong sentient area vasoconstriction, radiative heat loss quickly becomes far greater than heat production and core temperature falls at a rate ranging from 1.0 to 1.4°C per hour. A central metabolic shiver response occurs far more rapidly in these patients than in Case #1 - on an average of 50 minutes from the induction of spinal anesthesia. Core temperature at the beginning of shivering had fallen substantially in 2 of the 3 patients 0.9°C and 2.0°C but negligibly (0.1°C) in the third.

Thermal comfort data comparing cortical appreciation of temperature change to actual temperature change suggests that cerebral perception precedes cutaneous thermal change. Such a system would be of obvious behavioral benefit, especially to poikilotherms to enable the avoidance of thermal

TEMPERATURE - °C
ACTIVE CONSTANT SHIVER
BURSTS only
No FURTHER SHIVER
RECTAL
SKIN
AMBIENT
RECOVERY ROOM
OR #7
O.R. #5

Figure 5

extremes before net heat gain or heat loss became significant.[11]

The reproducible correlation between sensory level of spinal anesthesia (T_7--T_9 to cold in all cases) and reestablishment of cutaneous vasoconstriction in the foot is a surprising finding. Sympathetic nervous innervation to the foot is lumbar in origin. Cold sensation level closely approximates level of sympathetic blockade.[14] The decrease in foot temperature occurs hours after the introduction of sympathetic blockade making it difficult to invoke vascular stasis as the cause of the abrupt cutaneous temperature change. A vasomotor response is undoubtedly occuring, but its neurological pathways are, at present, obscure.

This experiment has yielded data in support of the temperature regulation classicists who champion the theory of multiplicative peripheral and central thermal drives eliciting homeostatic effector responses. Further studies shall be undertaken to evaluate, in particular, the thermal course of low spinal anesthesia cases. Core temperature decreases under low spinal anesthesia is less rapid and less intense than under high spinal anesthesia due to heat conserving vasoconstriction in the larger sentient body. This dampens the thermal stress and allows for a clearer appreciation of the input from the peripheral cutaneous sensors. The data presented also suggests a tentative hypothesis involving a biphasic effector response to moderate cold stress.

One of Benziger's most compelling arguements for his theory of strict central mediation of thermoregulation is that the skin cannot be both a sensory and effector organ without introducing a positive feedback loop into the controlled system. He then argues that the skin is solely an effector organ--an untenable view to most investigators in the field. Case #1, with its dampened thermal stress, offers a tentative model where-

by a relatively small and gradual decrease in hypothalamic temperature secondary to net body heat loss elicits peripheral vasoconstriction as a thermoeffector response. The second phase of this schema would have the resulting fall in skin temperature trigger a shiver response. By envisioning the skin as a sensory organ involved in a separate systems loop from its function as an effector organ, one can satisfy physiological evidence as well as engineering analysis.

APPENDICES

CONSENT FORM

I agree to participate in the temperature regulation study under spinal anesthesia. I understand that I shall be receiving the usual medications for anesthesia and that I shall be given no additional medications for this study. Temperature probes will be taped onto my body to measure skin temperatures. Central temperatures will be taken by rectal thermometer.

Date _____

Signed _____

Weighting Factors

(from the Brookline Instrument Company manual for the Brookline Temperature Computor)

Each of the eight skin probes has an individual weighting factor associated with it. For normal subjects, the appropriate factors are as follows:*

1.	Face, cheek	3
2.	Arm, upper outer ..	6
3.	Hand, top of	3
4.	Front, chest	7
5.	Back	7
6.	Thigh, outer	7
7.	Calf, outer	5
8.	Foot, top of	3

* Hardy, J. D. and DuBois, E. F., The Technic of Measuring Radiation and Convection. Journal of Nutrition, Volume 15, No. 5, Pages 461-475, 1937.

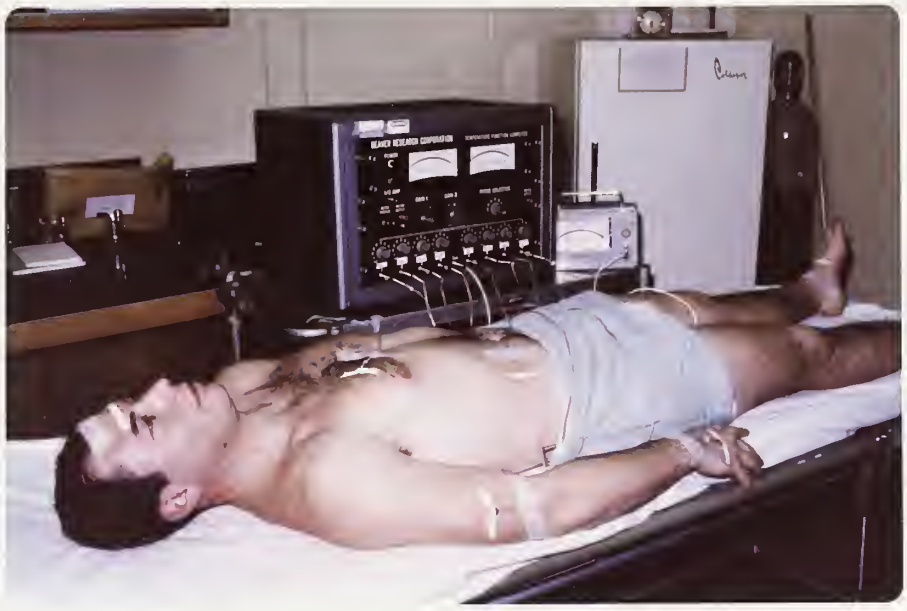
PHOTOGRAPHS

Photograph 1

Brookline Temperature Computor
Beaver prototype

Photograph 2

Brookline Thermometer
(portable)



Photograph 3 Author and Instruments

Photograph 4 Closeup of ETC thermistor probe attachment to skin--note firm attachment with minimal tape and collodion

Photograph 5 Sensory level of spinal anesthesia to cold sensation--ether soaked gauze lightly applied to skin

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